

REMARKS

Claims 23-27 are pending in this application.

Claims 23-27 stand rejected as unpatentable over U.S. Pub. 2002/0022622 (“Wagle”) in view of *Intl. J. Pharmaceutics*, 33 (1986) 201-217 (“Gould”). The Examiner acknowledges that 2-amino-4,5-dimethylthiazole is not disclosed by Wagle but states that “two closely related compounds are specifically stated which are 2-amino-5-methylthiazole and 2-amino-4-methylthiazole.” The Examiner states that it “is well established that the substitution of methyl for hydrogen on a known compound is not a patentable modification absent unexpected or unobvious results.” [OA, at p. 4]. Applicants traverse this rejection.

The Examiner relies on the alleged structural similarity between 2-amino-4,5-dimethylthiazole and Wagle’s 2-amino-5-methylthiazole and 2-amino-4-methylthiazole compounds to contend that “there is a prima facie case of obviousness because of the close structural similarity between the present composition and the composition of the prior art, [and] there is a presumed expectation that such compounds possess similar properties.” Again, the Examiner has offered no rationale as to why one skilled in the art would have been motivated to modify the compounds of Wagle. The Federal Circuit has rejected the approach taken by the Examiner and emphasized that a specific motivation to make the claimed compound is required, even in the case of obviousness based on structural similarity:

A known compound may suggest its homolog, analog, or isomer because such compounds “often have similar properties and therefore chemists of ordinary skill would ordinarily contemplate making them to try to obtain compounds with improved properties.” We clarified [in *In re Deuel*, 51 F.3d 1552 (Fed. Cir. 1995)], however, that in order to find a prima facie case of unpatentability in such instances, a showing that the “prior art would have suggested making the specific molecular modifications necessary to achieve the claims invention” was also required.

Takeda Chemical Indus. v. Alphapharm, 492 F.3d 1350, 1356 (Fed. Cir. 2007) (emphasis added). Applicants submit that the rejection is deficient for at least the reason that the Examiner has yet to articulate any rationale that would have motivated one skilled in the art, with a reasonable expectation of success, to modify the compounds of Wagle to arrive at the claimed compound.

Moreover, Applicants submit that 2-amino-4,5-dimethylthiazole is not obvious over 2-amino-5-methylthiazole or 2-amino-4-methylthiazole because the unpredictability in the art would have precluded one skilled in the art from concluding that the instantly claimed compound has similar properties to Wagle's compounds. See In re May, 574 F.2d 1082 (CCPA 1978). Indeed, the MPEP requires that the Examiner must "[c]onsider the predictability of the technology" because if "the technology is unpredictable, it is less likely that structurally similar species will render a claimed species obvious because it may not be reasonable to infer that they would share similar properties." MPEP §2144(II)(A)(4)(e). The Examiner has characterized the instant art, on the record, as "**an unpredictable and undeveloped art**" in connection with an enablement rejection (See April 18, 2007 OA, at p. 4) and should not now take an inconsistent position merely because it is expedient to do so to frame an obviousness rejection.

The state of the art at the time the instant patent application was filed would have precluded a reasonable expectation that the claimed compound would have similar properties to Wagle's compounds. For example, Applicants provide herewith a copy of an article by Musah et al. titled "Artificial Protein Cavities as Specific Ligand-binding Templates: Characterization of an Engineered Heterocyclic Cation-binding Site that Preserves the Evolved Specificity of the Parent Protein" (*J. Mol. Biol.* (2002) 315, 845-857) which illustrates the dramatic differences in binding efficiency between 2-amino-5-methylthiazole or 2-amino-4-methylthiazole in the active site of the W191G mutant of cytochrome *c* peroxidase. As shown in Table 1 of Musah, 2-amino-5-methylthiazole had the strongest ligand-protein interaction of the 34 heterocyclic ligands investigated, with a dissociation constant K_d of 0.006 mM. By comparison, the binding of 2-amino-4-methylthiazole was over an order of magnitude weaker, giving a dissociation constant of 0.23 mM. Also of note is the fact that 2-aminothiazole -- which lacks methyl groups altogether -- gave an intermediate K_d of 0.04 in this binding model of cytochrome *c* oxidase, which is an order of magnitude weaker binding than 2-amino-5-methylthiazole, but five-fold superior to 2-amino-4-methylthiazole. Applicants submit that this example from the literature illustrates that the binding of 2-amino-4,5-dimethylthiazole is not obvious over 2-amino-5-methylthiazole or 2-amino-4-methylthiazole because one skilled in the art would not have expected these compounds to possess similar properties. Indeed, inasmuch as Wagle's compounds do not have similar activities to one another in this enzyme model, it is not seen how 2-amino-4,5-dimethylthiazole could reasonably be expected to have similar properties to them.

Based on the foregoing, Applicants submit that the present claims are not obvious over Wagle, taken alone or in combination with Gould, on which the Examiner relies only for the teaching of hydrochloride salts generally. Having distinguished independent claim 23 from the art of record, Applicants submit that the claims dependent therefrom are patentable for at least the same reasons but reserve the right to separately argue the patentability of those claims in the future, if necessary.

CONCLUSION

Applicants respectfully submit that the instant application is in condition for allowance. Entry of the amendments and an action passing this case to issue is therefore respectfully requested. In the event that a telephone conference would facilitate examination of this application in any way, the Examiner is invited to contact the undersigned at the number provided.

Respectfully submitted,

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